



The Incidence of Concomitant Precancerous Lesions in Cases Who Underwent Hysterectomy for Prolapse

Prolapsus için Histerektomi Yapılan Olgularda Eşlik Eden Prekanseröz Lezyonların İnsidansı

Hysterectomy Histopathology

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Özet

Amaç: Çalışmanın amacı pelvik organ prolapsusu nedeniyle histerektomi yapılanlarda beklenmedik jinekolojik kanseri ve prekanseröz lezyonların insidansını belirlemek böylece uterus koruyucu cerrahinin risklerini anlayabilmektir. **Gereç ve Yöntem:** Bu uterin prolapsus cerrahisi öncesi servikal sitoloji, transvajinal ultrasonografi ve yüksek risklilere (endometrial kalınlığı ≥ 5 mm olan postmenopozal kadınlar ve anormal uterin kanamalı premenopozal kadınlar) uygulanan endometrial histopatolojik incelemenin yer aldığı preoperatif değerlendirme yapılan histerektominin histopatolojik bulgularının retrospektif analizidir. Endometrial, servikal veya ovaryan kanser veya prekanseröz lezyon öyküsü bulunan hastalar ve eksik tıbbi kayıtları olan kadınlar çalışmaya dahil edilmedi. **Bulgular:** Histerektomi yapılan 106 kadın vardı. Abdominal yol 22 (%21.7) vakada, vajinal yol 82 (%77.4) vakada ve laparoskopinin asiste ettiği vajinal histerektomi iki (%1.9) vakada kullanıldı. Vakaların 35'inde (%33) ooferektomi uygulandı. Histerektomi materyallerinden hiçbirinde malign histopatoloji tespit edilmedi. Premalign patoloji insidansı %7.5 (8/106) olarak bulundu. Altı kadında (%5.7) basit atipisiz endometrial hiperplazi tespit edilirken 2 kadında (%1.9) servikal intraepitelyal neoplazi tespit edildi. **Tartışma:** Transvajinal ultrasonografi ve yüksek riskli vakalara endometrial patolojik incelemenin dahil olduğu preoperatif değerlendirme sonrasında histerektomi yapılan kadınlarda endometrial, servikal ve ovaryan malinite insidansı yok denecek kadar azdır. Düşük riskli endometrial ve servikal prekanseröz lezyonların dahil edilmesi ile insidans artar. Bizim sonuçlarımız uterus koruyucu prolapsus cerrahisi isteyen benzer popülasyona yansıtılabilmesi için önemli bilgiler sunar.

Anahtar Kelimeler

Histerektomi; Histopatoloji; Prekanseröz; Prolapsus

Abstract

Aim: The aim of the study was to assess the incidence of unexpected gynecological cancers and pre-cancerous lesions following hysterectomy for pelvic organ prolapse to better understand the risks of uterine sparing surgery. **Material and Method:** This was a retrospective analysis of histopathology findings after hysterectomy for uterine prolapse surgery who underwent preoperative diagnostic work including cervical cytology, transvaginal ultrasonography and endometrial histopathological examination for a high risk group (Postmenopausal women with an endometrial thickness of ≥ 5 mm and premenopausal women with abnormal bleeding). Patients with a history of endometrial, cervical and/or adnexal precancerous or cancerous pathological conditions and with incomplete medical records were excluded. **Results:** Results were taken from 106 women who underwent hysterectomy. The abdominal route was used in 22 cases (21.7%), the vaginal route in 82 patients (77.4%) and laparoscopic-assisted vaginal route in two (1.9%) women. Oophorectomy was performed in 35 (33%) cases. None of the patients had malignant histopathology specimens from hysterectomy. Total premalignant pathology incidence was 7.5% (8/106). Six (5.7%) patients had simple endometrial hyperplasia and 2 patients (1.9%) had cervical intraepithelial neoplasia. **Discussion:** The incidence of unexpected endometrial, cervical or ovarian malignancy among women who underwent hysterectomy after preoperative diagnostic workup including transvaginal ultrasonography, endometrial pathological examination to high risk cases was negligible. The inclusion of low risk endometrial and cervical precancerous lesions increased the incidences. Our results could provide precious data to extrapolate to similar populations with uterine prolapse who desire surgical correction sparing uterus.

Keywords

Hysterectomy; Histopathology; Precancerous; Prolapse

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Introduction

The most common gynecological operation performed worldwide is the hysterectomy [1]. Leiomyomas, abnormal heavy menstrual loss, uterine prolapse, cancer and precancerous lesions in reproductive organs, chronic pelvic pain, endometriosis and pelvic inflammatory disease are frequent indications for hysterectomy. In most cases, hysterectomy is performed to relieve symptoms and improve quality of life. There is an ongoing debate about hysterectomy in the axis of need for hysterectomy, route (robotic, laparoscopic or vaginally), usage of morcellation and total or subtotal. There are many suggestions from the media to avoid hysterectomy, which is the number one surgery women may not need, like episiotomy and heartburn surgery [2]. The decision to perform hysterectomy or not depends on several factors: age, completion of child-bearing, race, cultural beliefs, and whether one is the patient or the surgeon. The anticipated benefits of removing the uterus with or without adnexes must be carefully weighed against the possible risks of surgery and other alternative treatments [3].

Uterovaginal prolapse (UVP) is defined as the descent of the uterus or apex of the vagina into the anterior or posterior vaginal wall. It is particularly common among parous women, with an estimated prevalence ranging from 37 to 50 % [4, 5]. It leads to impaired quality of life (QoL), with a substantial impact on bladder, bowel and sexual function [6]. The estimated prevalence of pelvic organ prolapse (POP) is between 37% to 50%. Hysterectomy, most commonly vaginal hysterectomy is a frequently carried out operation for POP and is usually combined with other reconstructive or anti-incontinence procedures even when uterine diseases or precancerous lesions are not present [7]. During the last decade there is a renewed interest among surgeons and patients in uterine conservation at the time of UVP surgery. Prolapse of the uterus is the result and not the cause of the apical prolapse and uterus conservative surgery is related with fewer complications, fast postoperative recovery and fewer bladder symptoms [8]. Another concern is to reduce the risk of gynecologic cancers by removing the uterus with or without the ovaries.

In the literature there are only a few reports of missing gynecological cancer in cases of hysterectomy for POP [9-12]. This study aims to assess the incidence of a malignant and/or premalignant, cervical and ovarian pathological condition in women undergoing hysterectomy for POP, who were otherwise asymptomatic, with normal cervical screening and who had undergone a normal transvaginal ultrasound (TVU) scan.

Material and Method

This is a retrospective study of patients who underwent hysterectomy for uterine prolapse between July 2011 and December 2015, in Bezmialem Vakif University, Istanbul, Turkey. As this is a non-interventional observational study, formal ethical approval was not obtained. The demographic data including age at surgery, parity, a history of previous miscarriage, smoking, menopausal status, the preoperative clinical diagnosis, the histopathology of the endometrium obtained by dilatation and curettage (D&C) when available, the final histopathology results of the hysterectomy specimens and cervical cytology results were all retrieved from the medical records and/or the central

ized computer system by the authors.

Clinical details, such as medical tests, postmenopausal or abnormal vaginal bleeding and the gynecological examination were recorded. Postmenopausal status was defined as amenorrhea for more than one year since the last menstrual period. TVU is routinely performed in all women and endometrial thickness was measured using TVU before the surgery. A history of medical conditions, including hypertension, diabetes mellitus, hypercholesterolemia and thyroid disease, were recorded if the hospital records confirmed the diagnosis. Body mass index (BMI) was calculated as weight divided by the square of height. Postmenopausal women who were found to have an endometrial thickness of ≥ 5 mm on TVU and premenopausal women with abnormal uterine bleeding, irrespective of the endometrial thickness, underwent D&C. The diagnosis of an abnormal cervical cytology test was based on the documentation of pathology results. In all cases a hysterectomy was performed via transvaginally, abdominally or laparoscopy assisted vaginal route. The vaginal vault was suspended either abdominally (sacrocolpopexy) or transvaginally (uterosacral ligament suspension). Bilateral salpingo-oophorectomy was performed when ovaries were accessible in women wishing to have their ovaries removed. Colposuspension or midurethral sling (MUS) procedures were performed in cases of coexisting stress urinary incontinence, which was confirmed with cough stress test. All specimens underwent microscopic histopathological examination. Patients with a history of endometrial, cervical and/or ovarian precancerous or cancerous pathological conditions and with incomplete medical records were excluded.

Statistical analyses were performed using the statistical package for the Social Sciences, version 21 (SPSS, Chicago, IL). Descriptive statistics of data were reported as mean \pm SD, range, percentage and 95 % confidence intervals (CIs).

Results

During the study period, a total of 111 women with UVP underwent hysterectomy. Three patients with a history of recent cervical dysplasia (2 patients with low-grade squamous intraepithelial lesion and one patient with high-grade squamous intraepithelial lesion), and two patients with a history of an adnexal mass were excluded. There were 106 women remaining who underwent hysterectomy via abdominal or vaginal route and had no known premalignant or malignant gynecologic pathology preoperatively for analysis. Mean age was 61.7 ± 8.3 years (range 43–77, 95 % CI=60–63.3), with a mean BMI of 29.7 ± 3.7 (range 24.3–37.3, 95 % CI=28.2–31.4). The majority of patients were postmenopausal (85 out of 106; 87.6 %).

For all the women, the demographic and gynecologic characteristics are shown in Table 1.

The abdominal route was used in 22 cases (21.7 %), the vaginal one in 82 patients (77.4 %) and laparoscopic-assisted vaginal route in two (1.9 %) women. A detailed description of the procedures performed is presented in Table 2. A total of 17 (16 %) patients underwent a sacrocolpopexy, whereas 29 (27.4%) patients had an anterior or posterior colporrhaphy, and 11 (10.4 %) women had an additional anti-incontinence operation. Oophorectomy either via abdominally or vaginally was performed

Table 1. Demographic and gynecological characteristics of the women who underwent hysterectomy for uterine prolapse.

Age at surgery (years)	Number of cases	Percentage (%)
40-50	9	8.5
51-60	40	37.7
>60	57	53.8
Parity		
Nulliparity	1	0.9
Primiparity	1	0.9
Multiparity	104	98.2
Cesarean delivery		
0	102	96.2
1 or more	4	3.8
Menopausal status		
Postmenopausal	94	88.7
Postmenopausal	12	11.3
Smoking	12	11.3

Table 2. Procedures at the time of hysterectomy

Procedure	N (%)
Hysterectomy, any	
Vaginal	22 (21.7)
Abdominal	82 (77.4)
Laparoscopic assisted vaginal	2(1.9)
Oophorectomy	
Abdominal	21 (60)
Vaginal	14 (40)
Colporrhaphy	
Anterior	9 (31)
Posterior	1 (3.5)
Anterior and posterior	19 (65.5)
Incontinence procedure	
Midurethral sling	4 (36.4)
Colposuspension	7(63.6)
Sacrocolpopexy	17 (16)

in 35 (33 %) of the women. Most of the abdominal hysterectomies were accompanied with salpingo-oophorectomy (20 out of 22) cases. A total of 14 bilateral salpingo-oophorectomies were performed concomitant to vaginal hysterectomy.

None of the patients had malignant histopathology from the specimens of the hysterectomy (Table 3). Total premalignant pathology incidence was 7.5 % (8/106; 95% CI, 2.8– 13.2). Six (5.7%; 95% CI, 1.9– 11.3) patients had unanticipated premalignant endometrial pathology, with simple hyperplasia. From cervical pathology, 2 patients (1.9 %; 95% CI, 0– 4.7) had cervical intraepithelial neoplasia (CIN1). Neither patient had a history of cervical dysplasia. No patients had CIN2-3 or cervical carcinoma.

The histopathology of the endometrium prior to hysterectomy was reported in the case notes of 35 cases (33%) due to postmenopausal endometrial thickness over 5mm, postmenopausal or menorrhagia. The most common finding was an unspecific endometrium change which was reported in 17 cases (48.6 %). Other findings include proliferative endometrium in 7 cases (20%), atrophic endometrium in 2 cases (5.7%), endometrial polyp in two cases (5.7%) and insufficient tissue in 5 cases

Table 3. Patients with abnormal histopathological findings. Data presented as n (%) unless otherwise noted. CIN; cervical intraepithelial neoplasia,a; mean (range)

Specimen	n (%)
Uterus (n =106)	
Volume (mm3)	173 (48-1147)a
Leiomyoma(s)	29 (27.4)
Adenomyosis	19 (17.9)
Leiomyoma(s) + Adenomyosis	8 (7.5)
Endometrium	
Endometrial polyp	9 (8.5)
Atrophy	41 (38.7)
Endometritis	1 (0.9)
Proliferation	28 (26.4)
Endometrial hyperplasia	
Simple	6 (5.7)
Complex	0 (0)
Complex with atypia.	0 (0)
Endometrial carcinoma	0 (0)
Cervix	
Inflammation	87 (82.1)
CIN I	2 (1.8)
CIN II-III	0 (0)
Cervical carcinoma	0 (0)
Ovaries (n=35)	
Simple serous cyst (over 3 cm)	4 (3.8)
Ovarian cancer	0 (0)

(14,3%). Most of the women underwent cervical cytological examination. In smear, 50 women (61%) had normal cytology, one (1.2 %) had atypical squamous cells of undetermined significance, 14 (17.1 %) had atrophy and 17 (20.7 %) had inflammatory changes.

With regard to benign disease, fibroid was the most common finding in uterine specimens reported in 29 cases (27.4%). Adenomyosis finding was reported in 19 (17.9 %) of the cases and adenomyosis and leiomyoma coexistence were found in 8 cases (7.5%). The most common finding in the endometrium of the uterine specimens was endometrial atrophy (38.7%, 41 out of 106 cases). Other findings include proliferative endometrium in 23 cases (21.7%), endometrial polip in 9 cases (8.5%) and atrophic endometritis in 1 case (0.9 %), endometrial polip in 2 cases (5.7%) and insufficient tissue in 5 cases (14,3%). There was no agreement between the preoperative endometrial pathology and final histopathological evaluation of hysterectomy specimens (Kappa = 0.29).

Discussion

In our study population the incidence of pre cancerous lesions of the endometrium and cervix found at the time of hysterectomy due to UVP was 7.5%. The incidence of cervical, endometrial and ovarian cancer was 0 %. All patients were asymptomatic with a negative diagnostic workup, including a preoperative TVS showing no gynecological abnormalities. Grigoriadis et al. and Frick et. al. reported the incidence of abnormal histopathological finding of the uterus as 4.2% and 2.6% , respectively among women who underwent vaginal hysterectomy for POP [10, 12].

In the literature the incidence of unanticipated cervical cancer among asymptomatic women who undergo a hysterectomy for UVP was 0.3%. Among 333 women Grigordiasis et al. reported 1 case of cervical cancer in a 71-year-old woman and another 1 (0.3%) with CIN3 in a 66-year-old patient with a normal smear. They reported 3 cases (0.9%) of CIN1 who also had had negative smear tests 6 months to 3 years before the operation [12]. Our 1.9% incidence of unanticipated CIN is compatible with the total 1.2% rate of this study. In another retrospective study Frick et al. reported no cervical cancer or CIN2/3 among 644 hysterectomy specimens; two patients had (0.3%) CIN1. The risk of cervical carcinoma has not been reported in uterus conserving prolapse surgery, but the rate of cervical carcinoma was low (below 0.3%) from studies evaluating supracervical hysterectomy of which can be extrapolated to uterine-sparing surgery [10]. Even in studies that predated modern cytological and viral screening techniques, the rate of cervical carcinoma was low (below 0.3%) [13]. With HPV vaccine and improved cytological and viral screening, this incidence rate is likely to be even lower. The incidence of unexpected endometrial cancer among asymptomatic women who undergo a hysterectomy for POP varies between 0 and 0.8% [9-12]. Renganathan et al. studied pathological specimens from 517 women who underwent vaginal hysterectomy for prolapse and found the rate of endometrial cancer to be 0.8% [9]. There was no information regarding the incidence of endometrial hyperplasia. They noted that whole cases of endometrial malignancy were in postmenopausal women and if premenopausal women are excluded the risk of endometrial cancer rises to 1.1%. They also emphasized the importance of preoperative TVU that they did not perform routinely.

Studies evaluating uterine pathology also demonstrate low risks for endometrial hyperplasia and cancer. In a retrospective study, Renganathan et al. studied pathological specimens from 517 asymptomatic women without abnormal uterine bleeding who underwent vaginal hysterectomy for prolapse and found the rate of endometrial cancer to be 0.8% [9]. Another retrospective trial evaluated the risk of unanticipated pathology at the time of hysterectomy for UVP among 681 pathological specimens. Frick et al. reported 0.8% simple hyperplasia, 0.5% complex hyperplasia, 1.1% complex hyperplasia with atypia, and 0.3% endometrial carcinoma [10]. Also in this study, none of the premenopausal women had premalignant or malignant pathology. The highest rate (13.3%) of missing endometrial pathology was seen in postmenopausal women with abnormal bleeding despite negative preoperative diagnostic evaluations. In a recent retrospective study evaluating the incidence of malignant and premalignant endometrial pathologies 2.7% of cases had endometrial hyperplasia [12]. They reported no cases of endometrial cancer. Three out of four cases of complex endometrial hyperplasia without atypia (1.2%) were found in postmenopausal women. Three out of four cases of simple endometrial hyperplasia (1.2%) and one case of complex endometrial hyperplasia with atypia (0.3%) were found in premenopausal women with endometrial thickness ranging from 6 to 7 mm. In our study we found 6 cases of simple hyperplasia, all of these cases were found in the postmenopausal period, with endometrial thickness ranging from 2.3 to 14 mm. Five out of six

cases underwent dilation and curettage before surgery and in all cases endometrial histopathology was negative for premalignant endometrial hyperplasia. This is particularly important when counseling women regarding uterus sparing procedures as simple endometrial hyperplasia without atypical symptoms, have a known risk of 1% to progress to endometrial carcinoma [14].

Currently, a noninvasive, cost-effective screening strategy does not exist for asymptomatic women desiring uterine-sparing surgery. Renganathan et al. suggested the usage of preoperative transvaginal ultrasonography in all cases to avoid the risk of missing an endometrial cancer, followed by endometrial sampling in women with increased endometrial thickness [9]. Using ultrasound as an isolated screening test may yield high false positive results. Ultrasound has been shown to have a sensitivity of 97% and specificity of 55% for the detection of endometrial cancer with an endometrial stripe of ≥ 5 mm [15]. This would yield a positive predictive value of 57% and a negative predictive value of 99.8%.

In contrast to women with postmenopausal bleeding, women without postmenopausal bleeding, using an endometrial thickness of ≥ 5 mm has a lower sensitivity and specificity for detecting endometrial cancer [16]. Also the absence of ovarian cancer in our series is consistent with previous reports underlining the usefulness of transvaginal ultrasonography as an investigation prior to prolapse surgery [2, 17]. In a study that evaluates the usefulness of transvaginal ultrasonography prior to vaginal hysterectomy Srikrishna et al. found gynecological pathology in 46.6% of patients and changed the planned management in 2.9% of cases due to large fibroids and ovarian cysts [18].

The strengths of our study come from the single institution data with all cases evaluated with transvaginal ultrasound, cervical cytology and endometrial sampling in cases of necessity. The major limitation is the retrospective design of the study could create selection bias and reliability of data regarding gynecological history. Another limitation was the relatively small size of the study population when assessment of the primary outcome of abnormal gynecologic histopathology was relatively rare. Limited numbers of cases with concomitant oophorectomy, given that ovaries were not systematically removed, must be considered when interpreting the data presented. Lastly, absence of consensus about the definition of abnormal endometrial thickness in asymptomatic postmenopausal women and the exclusion of cases with preoperative malignant or premalignant pathology limits the true incidence of precancerous or cancerous pathologies of patients who will undergo pelvic organ prolapse surgery.

In the present study, we evaluated the risk of unanticipated gynecological cancerous or precancerous pathology among women with a defined preoperative diagnostic workup including transvaginal ultrasonography, D&C according to increased endometrial thickness, and postmenopausal or pre-menopausal abnormal uterine bleeding. With this examination we did not find any cases of endometrial, cervical or ovarian malignancy. However, the inclusion of low risk endometrial and cervical precancerous lesions (simple endometrial hyperplasia and CIN1) increased the incidence to 7.5% (8 out of 106). Our results could be to ensure precious data is extrapolated to similar populations with utero-

vaginal prolapse who desire surgical correction. When uterus sparing procedures or procedures involving the conservation of part of the uterus, such as subtotal hysterectomy or ovaries are considered, this information is important during the consulting period. Currently, a cost effective screening strategy or diagnostic work up does not exist for a woman desiring uterine-sparing surgery. Future studies including a larger number of patients, larger number of specimens concomitant oophorectomies and studies that evaluate the incidence of malignancy after uterus sparing surgery are needed to provide more robust evidence.

Competing interests

The authors declare that they have no competing interests.

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